REMARKS

Claims 1-9 are pending and under consideration in the instant application. With this response, the specification and Claim 1 have been amended. After entry of the instant amendment, Claims 1-9 are pending and under consideration. A version with markings to show changes made to the specification is attached at Exhibit A. A version with markings to show changes made to Claim 1 is attached at Exhibit B. For the Examiner's convenience, a clean copy of all pending claims is attached at Exhibit C.

I. THE AMENDMENT OF THE SPECIFICATION

The specification on page 13, lines 17 to 34; page 19, line 32 to page 21, line 23; page 24, lines 1 to 12; page 36, lines 6 to 9 and the abstract on page 48, have been amended to correct minor grammatical errors and to describe, in relevant part, that one primer binds to a first binding sequence A′ which is essentially complementary to A and the other primer binds to a second binding sequence C which is located in the 3′ direction from A and does not overlap A. The amendments of the specification are supported by the specification, for example, at page 44, line 16 to page 45, line 5 and Figs. 2, 6 and 7. For example, Fig. 2 depicts the amplificate as comprising sequences A, B and C, wherein C is located in the 3′ direction of A. Also depicted is the complement of the amplificate comprising sequences A′, B′ and C′. To produce such an amplificate, the primers bind to sequences A′ and C (not A and C′) as pointed out by the Examiner. The Example provided in the specification, and Figs. 6 and 7 demonstrate the correct directionality of binding sequences A and C′. For instance, Fig. 6 provides a section of the HCV genome from positions 261 to 333 in the 5′ to 3′ direction. The forward primer (for example, CK10) is essentially identical to the sequence at the 5′ region and the reverse primer (CK20) is complementary to the sequence at the 3′ region. The forward primer, CK10, binds to the complementary strand of the HCV strand provided, corresponding to binding sequence A′. The reverse primer, CK20, binds to binding sequence C, which is essentially complementary to binding sequence C′ and binding sequence C being in the 3′ direction from A.

Given the support in the specification, including the examples and figures, the amendments to the specification do not introduce new matter. Entry of the amendments is respectfully requested.

II. THE AMENDMENT OF THE CLAIMS

Claim 1 has been amended to recite a method for the detection of a nucleic acid comprising: (a) producing a plurality of amplificates of a section of the nucleic acid by amplifying said section of nucleic acid with two primers, one of which binds to a first binding sequence A′ of one strand of the nucleic acid, wherein said binding sequence A′ is essentially complementary to a sequence A, located on the other strand of the nucleic acid, and the other primer binds to a second binding sequence C, which is located in the 3′ direction from A and does not overlap A, in the presence of a probe having a binding sequence D which binds to a third sequence B located between the sequences A and C or to the complement thereof, wherein the probe contains a reporter group and a quencher group, using a polymerase having 5′ nuclease activity; and (b) detecting the nucleic acid by measuring a signal which is caused by the release of the reporter group, wherein the amplificates have a length of 75 nucleotides or less, and the sequences located between the binding sequences A and C contains no nucleotides that do not belong to a sequence region E of the amplificate that is bound by binding sequence D of the probe.

Support for amended Claim 1 can be found in the specification, for example, at page 44, line 16 to page 45, line 5 and Figs. 2, 6 and 7. Fig. 2 depicts the amplificate and complement of the amplificate that is produced by primers that bind to sequences A′ and C. The specification at page 44, line 16 to page 45, line 5 and Figs. 6 and 7 further support amended Claim 1 by describing the HCV genomic sequence and amplicon formed therefrom, along with primers for use in the examples. Applicants therefore respectfully request entry of the amendment into the record.

III. THE REJECTIONS UNDER 35 U.S.C. § 112, second paragraph

Claims 1-9 stand rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness. Specifically, the PTO alleges that A) Claim 1 is indefinite as to the resulting amplification product and B) Claim 1 is indefinite as to the terms 'aid of' and 'can bind'.

A. Amplification Product

Claim 1 has been amended, as discussed above, to recite the production of the resulting amplification product. Primers that bind to sequence A′ and C produce an overlapping product. Support for amended Claim 1 may be found, for example in the specification at page 44, line 16 to page 45, line 5 and Figs. 2, 6 and 7.

Applicants thank the Examiner for pointing out the error in Claim 1 and respectfully request that the rejection be withdrawn.

B. Alleged Indefinite Terms

The PTO alleges that the terms 'aid of' and 'can bind' are indefinite. Amended Claim 1 recites, in relevant part, producing a plurality of amplificates of a section of the nucleic acid by amplifying said section of nucleic acid with two primers one of which binds to a first binding sequence A′ of one strand of the nucleic acid, wherein said binding sequence A′ is essentially complementary to a sequence A, and the other binds to a second binding sequence C which is located in the 3′ direction from A and does not overlap A, in the presence of a probe having a binding sequence D which binds to a third sequence B.

The amendment to Claim 1 replaces the alleged indefinite terms with those suggested by the Examiner. Applicants thank the Examiner for her helpful suggestions for amending the claim and respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants thank the Examiner for her helpful comments and suggestions. Applicants submit that Claims 1-9 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same and passage of Claims 1-9 to issuance is therefore kindly solicited.

No fees are believed due in connection with this response. However, the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150 (Order No. 1803-302-999).

Respectfully submitted,

Date: March 27, 2003

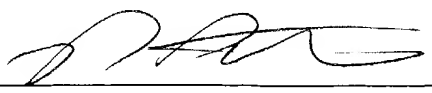

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EXHIBIT A

Specification Amendment: Version with Markings to Show Changes Made

On page 13, line 17:

The invention concerns a method for the detection of a nucleic acid comprising the steps of producing a plurality of amplificates of a section of [this] a nucleic acid with the aid of two primers, one of which can bind to a first binding sequence [(A)] (A') which is essentially complementary to a sequence A of a strand of the nucleic acid and of which the other can bind to a second binding sequence [(C')] (C) [which is essentially complementary to a sequence C] which is located in the 3' direction from A and does not overlap A, in the presence of a probe having a binding sequence D which can bind to a third sequence (B) located between the sequences A and C or to the complement (B') thereof, wherein this probe contains a reporter group and a quencher group, using a polymerase having 5' nuclease activity and detecting the nucleic acid by measuring a signal which is caused by release of the reporter group characterized in that the amplificates formed with the aid of the primers have a length of less than 100 nucleotides.

Page 19, line 32:

In the first essential step of the method according to the invention a segment of the nucleic acid to be detected is amplified. This segment is also referred to as an amplicon in the following. It is essential that this contains the sequence region between the outer ends of the [binding] sequences [A] A' and [C'] C or of the complement thereof [of the primers] (the primer binding regions) and contains the binding region E of the probe or of the complement thereof. According to the present invention the amplicon (preferably the total length of the sequences of the regions A, B and C) is preferably shorter than 100 nucleotides, particularly preferably shorter than 60 nucleotides, but preferably longer than 40 nucleotides. However, this does not mean that the total length of the amplificates cannot be larger e.g. when the primers have additional nucleotides that do not lie within the binding regions. Amplification methods are used which allow an amplification of the nucleic acid to be detected or the complement thereof and result in the formation of tripartite mini-nucleic acid amplification products [mini chain reaction (MCR)] (mini chain reaction (MCR)). In principle all nucleic acid amplification methods that are known in the prior art can be used for this. Target-specific nucleic acid amplification reactions are preferably used. Theoretically exponentional target-specific nucleic acid amplification reactions are particularly preferably used in which an anti-parallel replication of the nucleic acid to be detected or of its complement is carried

out e.g. elongation-based reactions such as the polymerase chain reaction (PCR for deoxyribonucleic acids, RT-PCR for ribonucleic acids). Thermocyclic exponential elongation-based nucleic acid amplification reactions are particularly preferred such as e.g. the polymerase chain reaction. The nucleic acids to be detected or complements thereof which are used for the amplification can be present in the form of single-stranded or double-stranded deoxyribonucleic acids or ribonucleic acids. The aim of the amplification reaction is to produce numerous amplificates of a segment of the nucleic acid to be detected. Hence an amplificate is understood as any molecular species produced by using sequence information of the nucleic acid. In particular the term refers to nucleic acids. The term "amplificate" includes single-stranded as well as double-stranded nucleic acids. In addition to the regions containing the sequence information of the underlying nucleic acid (amplicon), an amplificate can also contain additional regions which are not directly related to sequences of the nucleic acid to be amplified that are outside the ends of the primer binding sites which face away from another. Such sequences with a length of more than 15 nucleotides preferably do not occur on the nucleic acid to be detected or its complement and cannot hybridize with it by direct base pairing. Hence amplificates can either hybridize with the nucleic acid to be detected itself or with its complement. Amplificates are for example also products of an asymmetric amplification i.e. an amplification in which the two strands are formed in different amounts (e.g. by using different amounts of primers) or in which one of the two strands is subsequently destroyed (e.g. by RNase).

Page 24, line 1:

In the present invention the segment of the nucleic acid from which it is intended to produce a plurality of amplificates is selected such that it contains three regions A, B, and C. Regions A and C are regions selected such that one primer can use sequence [A] A′ as the binding sequence and the complement of the region [C] C′ can serve as the binding sequence for the other primer. A complement within the sense of the present invention is understood as a nucleic acid or nucleic acid sequence which is essentially complementary to a certain other nucleic acid e.g. a sequence region e.g. of an amplificate or of the nucleic acid to be detected.

Page 36, line 6:

The primers preferably bind to the binding sequences [A] A′ or [C'] C as described above and the probe preferably binds to a region B located between the ends of the binding sequences [A] A′ and [C'] C or to the complement thereof.

Page 48, line 2, abstract:

The invention concerns a method for the detection of a nucleic acid comprising the steps [production] of producing a plurality of amplificates of a section of [this] a nucleic acid having a length of less than 100 nucleotides with the aid of two primers, one of which can bind to a first binding sequence [(A)] (A') which is essentially complementary to a sequence A of a strand of the nucleic acid [of the nucleic acid] and the other can bind to a second binding sequence [(C')] (C) [which is essentially complementary to a sequence (C)] which is located in the 3' direction from (A) and does not overlap (A), which can bind in the presence of a probe with a binding sequence (D) which can bind to a third sequence (B) which is located between the sequences A and C or to the complement (B') thereof, wherein this probe contains a reporter group and a quencher group using a polymerase having 5' nuclease activity and detecting the nucleic acid by measuring a signal which is caused by the release of the reporter group.

EXHIBIT B

Claim Amendment: Version with Markings to Show Changes Made

1. (Five times amended) A method for the detection of a nucleic acid comprising:

(a)- producing a plurality of amplificates of a section of the nucleic acid [with the aid of], by amplifying said section of nucleic acid with two primers, one of which [can bind] binds to a first binding sequence [A] A′ of one strand of the nucleic acid, wherein said binding sequence A' is essentially complementary to a sequence A, located on the other strand of the nucleic acid, and the other [can bind] primer binds to a second binding sequence [C'] C, [which is essentially complementary to a sequence C] which is located in the 3′ direction from A and does not overlap A, in the presence of a probe having a binding sequence D which [can bind] binds to a third sequence B located between the sequences A and C or to the complement thereof, wherein the probe contains a reporter group and a quencher group, using a polymerase having 5′ nuclease activity; and

(b)- detecting the nucleic acid by measuring a signal which is caused by the release of the reporter group, wherein the amplificates have a length of 75 nucleotides or less, and the sequences located between the binding sequences A and C contains no nucleotides that do not belong to a sequence region E of the amplificate that is bound by binding sequence D of the probe.

EXHIBIT C

Claim Amendment: Pending Claims After Entry of Instant Amendment

1. (Five times amended) A method for the detection of a nucleic acid comprising:

   (a)- producing a plurality of amplificates of a section of the nucleic acid by amplifying said section of nucleic acid with two primers, one of which binds to a first binding sequence A′ of one strand of the nucleic acid, wherein said binding sequence A′ is essentially complementary to a sequence A, located on the other strand of the nucleic acid, and the other primer binds to a second binding sequence C, which is located in the 3′ direction from A and does not overlap A, in the presence of a probe having a binding sequence D which binds to a third sequence B located between the sequences A and C or to the complement thereof, wherein the probe contains a reporter group and a quencher group, using a polymerase having 5′ nuclease activity; and

   (b)- detecting the nucleic acid by measuring a signal which is caused by the release of the reporter group, wherein the amplificates have a length of 75 nucleotides or less, and the sequences located between the binding sequences A and C contains no nucleotides that do not belong to a sequence region E of the amplificate that is bound by binding sequence D of the probe.

2. The method of claim 1, wherein the binding sequence D of the probe does not overlap one of the binding sequences of the primers.

3. The method of claim 1, wherein at least one of the binding sequences is not specific for the nucleic acid to be detected.

4. The method of claim 1, wherein the total length of the amplificates formed with the aid of the primers have a length of less than 61 nucleotides.

5. The method of claim 1, wherein the probe is labeled with a fluorescence quencher as well as with a fluorescent dye.

6. The method of claim 1, wherein at least one of the primers is not specific for the nucleic acid to be detected.

7. The method of claim 6, wherein two of the primers are not specific for the nucleic acid to be detected.

8. The method of claim 6, wherein the probe is not specific for the nucleic acid to be detected.

9. The method of claim 1, wherein nucleotides which are complementary to A, G, C and T are used in the amplification.